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EXAMINER	
HAGHIGHATIAN, MINA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,408	DEBOECK ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/06/06 & 10/05/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim status

Claims 1-23 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Determination of Claim Scope

Claims 4 and 20-22 of the instant application claim a pharmaceutical composition comprising a formoterol or a solvate thereof.

Review of Applicants' Disclosure

The instant specification does not disclose, to which solvates of formoterol Applicants are referring. Applicants' specification does not disclose how to make any

particular solvate of formoterol, nor do Applicants depict chemical structures of formoterol as any particular solvate in their disclosure.

Possession Based on Ordinary Skilled Artisan's Determination/ State of the Prior Art

It is generally accepted in the art that the formation of a particular solvate (or hydrate) for a given compound or series of compounds is unpredictable (see Vippagunta et al. "Crystalline Solids," Advanced Drug Delivery Reviews, 2001, 48, pp 18), therefore, the generic reference to a solvate of formoterol in the instant specification does not provide adequate written support for claims drawn to any solvate of these compounds. An ordinary skilled artisan would conclude that Applicants were not in possession of any particular solvate of any of the compounds corresponding to formoterol of the claimed composition. Furthermore, because Applicants' generic reference to solvates of formoterol does not permit the ordinary skilled artisan to clearly envisage what specific solvatesl were in Applicants' possession, the only reasonable conclusion said artisan would make was that Applicants were not in possession of solvates of formoterol and had not reduced to practice the preparation, isolation, and characterization of said solvates and hydrates.

Claims 17-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Determination of Claim Scope

Claims 17-18 of the instant application claim a pharmaceutical composition comprising a propellant, wherein the propellant is a derivative of chloroflurocarbon or hydroclurocarbon respectively.

Review of Applicants' Disclosure

The instant specification does not disclose, to which derivatives of chloroflurocarbon or hydroclurocarbon Applicants are referring. Applicants' specification does not disclose how to make any particular derivatives of chloroflurocarbon or hydroclurocarbon.

Possession Based on Ordinary Skilled Artisan's Determination/ State of the Prior Art

It is generally accepted in the art that the formation of a particular derivative for a given compound or series of compounds is unpredictable, therefore, the generic reference to a derivative in the instant specification does not provide adequate written support for claims drawn to any derivatives of chloroflurocarbon or hydroclurocarbon.

An ordinary skilled artisan would conclude that Applicants were not in possession of any particular derivatives corresponding to chloroflurocarbon or hydroclurocarbon of the claimed composition. Furthermore, because Applicants' generic reference to derivatives of chloroflurocarbon or hydroclurocarbon does not permit the ordinary skilled artisan to clearly envisage what specific derivatives were in Applicants' possession, the only reasonable conclusion said artisan would make was that Applicants were not in possession of derivatives of chloroflurocarbon or hydroclurocarbon and had not reduced to practice the preparation, isolation, and characterization of said derivatives.

The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for reciting "composition for inhalation a fixed combination…". This appears to be a typographical error and should be corrected.

Regarding claim 5, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 7 as written includes the phrase "bronchodilator agent is tiotropium, oxitropium, ipratropium and mixtures thereof". Proper *Markush language* is "selected

from the group consisting of". The examiner suggests rewording the claim to include the Markush language. Note: MPEP 2111.03.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim **8** recites the broad recitation ratio of (A) to (B) is from 1:10 to 1:10000, and the claim also recites preferably from…..most preferably…." which is the narrower statement of the range/limitation. (NOTE: also in the claim, the term "10,000 is spelled 10,_000).

Claims 20-22 are indefinite for reciting "The composition or combination of claim 1, which is a dry powder inhaler…". The composition is not an inhaler, but the inhaler comprises the composition.

Note: In claim 10, the term "advantageously" is interpreted as "optionally". In claim 19, line 2, the term "or" allows for the alternative in the claim wherein the composition is either being a nebulizable composition or a solution/dispersion.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5, 8-12, 19 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over ZA940155 to Adcock Ingram limited (of South Africa) in view of Deboeck (US 4,847,282.

ZA940155 discloses pharmaceutical compositions comprising a) a therapeutic dose of acetylcysteine or carbocysteine or a pharmaceutically acceptable salt of acetylcysteine or carbocysteine; b) a therapeutic dose of terbutaline or a pharmaceutically acceptable salt of terbutaline; and c) one or more pharmaceutically acceptable excipients therefor. Preferably, ingredient (a) is acetylcysteine. Preferably, ingredient (b) is terbutaline sulphate. The pharmaceutical composition of the invention may be formulated as a capsule, a tablet, a syrup, an intravenous solution, a nebulizing solution, an aerosol inhaler, a dry powder inhaler or an aqueous pump spray. According to another aspect of the invention there is provided the pharmaceutical composition as described above for use in the treatment of respiratory tract disorders. Typically, the pharmaceutical composition is of particular use in treating coughs, bronchitis or chronic congestion as is present in emphysema (see pages 1-4).

Typically, the acetylcysteine is provided in an amount of 100 to 2000 µg except in the case of a nebulizing solution or an aerosol or dry powder inhaler or an aqueous pump spray where the acetyleysteine is provided in an amount of 100 – 2000 µg. The

terbutaline or terbutaline sulphate is typically provided in an amount of 1 – 10 mg except in the case of an aerosol or dry powder inhaler or aqueous pump spray where it is provided in an amount of 100 – 1000 µg (see page 4).

The specific formulations have been exemplified as a Nebulizing solution comprising Acetylcysteine at 100 µg -2000 µg and Terbutaline S04 at I mg-10mg, Alkali/buffer, Isotonicity agents at 5-100mg and Stabilisers, solubilisers at 0-100mg. Additionally, aerosolized inhalers, dry powder inhalers and aqueous pump sprays may contain Acetylcysteine at 100 µg -2000 µg and Terbutalin SO4 at 100 µg- 1000 µg (see page 6).

ZA940155 discloses that acetylcystein or a pharmaceutically acceptable salt thereof for the said formulations are suitable but lacks disclosure on the specific salts. However, this deficiency is cured by Deboeck '282.

Deboeck discloses mucolytic acetylcystein salts. Deboeck discloses the followings:

> Water-soluble acetylcysteine salts, useful as mucolytic agents, consisting of reaction products of acetylcysteine with at least one basic amino-acid, the latter being preferably selected from the group comprising arginine, lysine, histidine, ornithine and glycine.

(see abstract page).

The basic amino-acid or amino-acids used may be natural or not, such as, for example arginine, lysine, histidine, ornithine or glycine. The basic amino-acids according to the invention can include one or more asymmetrical centers and in this connection they can exist as optically active isomer forms. It should be cleary understood that the invention includes both epimer forms, such as the levorotary and dextrorotary forms, as well as mixture thereof. Examples of levorotary and extrorotary basic amino-acids are D- and L-lysines and D- and L-arginines. (see col. 1 ,lines 42-52)

The salts of the present invention may also be administered as aerosals or sprays, acetylcysteinate being either dissolved in a suitable solvent or as a powder. (see col .4 ,lines 3-5).

The active compound may be administered alone or in combination with other active products having a similar or different activity.

The recommended doses are, for example, 100 mg to 20 g, advantageously 500 ml to 10 g per day orally and rectaly. (see col. 4 ,lines 11-16).

In Examples 1 and 2 Deboeck discloses that lysine is added to a solution of acetylcystein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the L-lysine salt of N-acetylcystein as the salt of acetylcystein of powder or aerosol formulations of ZA940155 as it is disclosed by Deboeck that such salt possesses important advantages over other salts e.g. they cause much less bronchospasm. Thus one of ordinary skill in the art would have been motivated to have selected the specific salt as taught by ZA940155 for its advantages.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of

ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

With regards to the concentration ranges of active agents, MPEP 2144.05 stats that "[W]here the general conditions of a claim are disclosed in the prior art, it is **not** inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Claims 1-19, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deboeck (US 4,847,282) in view of Vanderbist et al (EP0876814) and in further view of Horstman et al (US 20040009963).

Deboeck, discussed above, lacks specific disclosure on addition of the bronchodilator, pressurized metered dose inhalers, DPI's multidose and monodose and lactose. However, these deficiencies are cured by Vanderbist et al and Horstman et al.

Vanderbist et al discloses the DPI composition containing L-lysine N-acetylcysteinate (see page 4, line 31) along with a lactose carrier (see page 2, line 45). Furthermore, the ideal inhalation device is simple to use, cheap and multidose (see page 2, line 36) although there are three kinds of devices such as nebulizers, pressurized metered dose inhalers (PMDIs) and dry power inhalers (see page 2, lines 9-10). Vanderbist teaches that there are two types of DPIs 1) monodose DPIs and 2) multidose DPIs (see page 2, lines 20-24). Vanderbist et al also teach that the formulations may contain a combination of active agents such as mucolytics, sympathomimetics, etc. A specific mucolytic agent is **L-lysine N-acetylcysteinate** (see page 4, lines 29-35). In addition, pressurized metered dose inhalers may contain HFAs gases (hydrofluoroalkanes) besides CFCs gases (see page 2, line 16-17).

Horstman et al teach formulations for inhalation comprising salmeterol and fluticasone for treating respiratory disorders such as COPD. Salmeterol is administered in a dose of from **50** to 2000 µg (see [0001], [0012] and [0013]). The said formulations may be in the form of a powder preferably with lactose or an aqueous solution of suspension delivered with the use of propellants such as dichlorodifluromethane, 1,1,1,2-tetrafluroethane, etc (see [0017]). The formulations may be delivered by way of a capsule containing powder medication and lactose (see [0020]). The formulations may contain other active agents such as tiotropium, ipratropium, a mucolytic, etc (see [0022]).

Both Deboeck and Vanderbist et al disclose DPI composition containing L-lysine N-acetylcysteinate. Both prior art commonly teach L-lysine N-acetylcysteinate composition can be administered as aerosols or multidose-inhalers. From these guidance, it would have been obvious to the skilled artisan in the art at the time of the invention to have incorporated the Vanderbist's et al lactose and multidose inhaler into the Deboeck's formulation in order to develop simply useable, cheap and multidosing inhalers by a routine experimentation. This is because the skilled artisan in the art would have expected such a modification to be acceptable and suitable in the art of the pharmaceutical industry. Horstman et al teach aerosol formulations comprising a variety of medicaments for treatment of respiratory disease. In other words, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

With regards to the concentration ranges of active agents, MPEP 2144.05 stats that "[W]here the general conditions of a claim are disclosed in the prior art, it is **not** inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck

& Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Claims 1-14, 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth (WO 9703649) in view of Vanderbist et al (EP0876814).

Staniforth teaches a powder for use in a dry powder inhaler comprising active material and additive material (see abstract). The suitable additive materials include N-acetyl-L cystein (see page 9, lines 25-37). The powder formulations are delivered to the patients lung by a dry powder inhaler. The active agents suitable for the said powder formulations and treatment of respiratory disorders include salbutamol, salmeterol, terbutaline, ipratropium bromide, sodium cromoglycate, etc (see page 11, lines 1-20).

Examples 1-7 disclose the amount of active and additive material in the formulation. The active material is from about 100-500 µg and the additive is from about 1 to 5 µg.

Staniforth teaches that L salts of N-acety cystein are suitable but lacks disclosure on the specific salt as claimed. However this is remedied by Vanderbist.

Vanderbist et al, discussed above, teach dry powder formulations comprising lactose and active agents. It is taught that the formulations may contain a combination

of active agents such as mucolytics, sympathomimetics, etc. A specific mucolytic agent is **L-lysine N-acetylcysteinate** (see page 4, lines 29-35).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the L-lysine salt of N-acetylcystein as the salt of acetylcystein of powder formulations as it is disclosed by Vanderbist in the formulations of Staniforth because Vanderbist teaches it to be an effective and suitable mucolytic agent. One of ordinary skill in the art is motivated to combine the L-lycine N-acetylcystein with any other bronchodilator because it can be both the mucolytic agent and the additive.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

With regards to the concentration ranges of active agents, MPEP 2144.05 stats that "[W]here the general conditions of a claim are disclosed in the prior art, it is **not** inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of

percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Claim 15-20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth (WO 9703649) in view of Vanderbist et al (EP0876814) as applied to the claims 1-14, 21 and 23 above and in further view of Keller et al (6,475,467).

Staniforth and Vanderbist have been discussed above. The combination lacks specific disclosure on specific active agents of formoterol and tiotropium and pressurized metered dose inhalers and propellants. These deficiencies are cured by Keller et al.

Keller et al teach medicinal aerosol formulations for inhalation and treatment of respiratory disorders. The active agents exemplified include a combination of formoterol fumarate and disodium cromoglycate (Examples 1, 6 and 10), tiotropium and nedocromil sodium (Example 7) and salmeterol xinafoate and disodium cromoglycate (Example 8).

Keller et al also teach use of N-acetylcysteine as a buffering and stabilizing agent. It is used in an amount of from 0.0001 to 1% of the formulation (see col. 9, lines 29-36). Suitable propellants are recited as HFAs, but Keller et al disclose that CFCs,

while not preferred, they are well known in the art (see col. 1). Keller et al also disclose the suitable concentration ranges and ratios of active agents (see col. 6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the L-lysine salt of N-acetylcystein as the salt of acetylcystein of powder formulations as it is disclosed by Vanderbist in the formulations of Staniforth because Vanderbist teaches it to be an effective and suitable mucolytic agent. One of ordinary skill in the art is motivated to combining the L-lycine N-acetylcystein with any other bronchodilator because it can be both the mucolytic agent and the additive. Furthermore, it would have been obvious to one of ordinary skill in the art to have selected other active agents such as formoterol and tiotropium as taught by Keller et al in order to provide the same benefit to many patients.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

With regards to the concentration ranges of active agents, MPEP 2144.05 stats that "[W]here the general conditions of a claim are disclosed in the prior art, it is **not** inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to

improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **1-7 and 23** are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 8, 9, 16, 48 of copending Application No. US 20060254583 (10/549,124). The provisional

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims would have been obvious over the reference claims. Here, instant claims are drawn to a pharmaceutical formulation for inhalation comprising a combination of two active agents, wherein one of the active agents is L-lycine N-acetylcystinate and the other is a bronchodilator. The formulations may in a pressurized aerosol comprising a propellant, or in a powder form. The reference claims are also drawn to a pharmaceutical formulation for inhalation comprising a combination of active agents. The reference claims require the active agent be selected from active agents such as mucolytics, bronchodilators, corticosteroids, etc. The difference is that instant claims require one of the active agents to be L-lycine N-acetylcystinate. The reference claims are broader. However in depending claims such as 9 and 48, the active agents is claimed as L-lycine N-acetylcystinate. It would have been obvious to have selected the combination of L-lycine N-acetylcystinate and a bronchodilator in the instant claims as they are of limited choices in the reference claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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